

Pharmacokinetics in Infants

Drug actions in infants are variable because of the infant's physiological attributes: small body mass, high relative body water content, low body fat, greater membrane permeability of the skin, and blood-brain barrier and reduced plasma-binding abilities.

Absorption:

Rates of drug absorption in the infant are lower than absorption rates in children and adults.

- Prolonged gastric transit time and variable gastric pH lead to diminished absorption.
- Frequent feedings impede absorption because the stomach is often full and the drugs must compete with nutrients for absorption.
- Low levels of intestinal flora and reduced enzyme function, both of which are necessary for active transport of some drugs, can result in decreased absorption.
- Low peripheral perfusion rates and immature heat regulatory mechanisms can also decrease absorption when drugs are given IV, IM, or SC.

Distribution:

Rates of drug distribution in the infant are higher than the distribution rates in children and adults.

- Infants have a low concentration of plasma proteins and a decreased plasma-binding capacity. Drugs that are less bound to proteins in infants are more available in the circulation to exert their pharmacological effects.
- Immature glial cell development results in greater permeability of the blood-brain barrier, allowing rapid access to drugs to the central nervous system.
- Total body water (TBW) is 80% of body weight for pre-term infants. (This is compared to 50% of body weight for adults). This increased body water content results in increased volume of distribution for water-soluble drugs.

Metabolism:

Rates of drug metabolism in the infant are lower than the metabolism rates in children and adults.

- Drug-metabolizing enzymes in the liver of infants are immature. Drugs are not biotransformed in inactive compounds as readily as they are in children and adults, resulting in higher levels of circulating active drugs and greater potential of toxicity.

Excretion:

Rates of drug excretion in the infant are lower than the excretion rates in children and adults.

- Infant kidneys have a higher resistance to blood flow, incomplete Loop of Henle's, incomplete glomerular and tubular development, low glomerular filtration rate, and decreased ability to concentrate urine. As a result, drugs are excreted more slowly, drug accumulation can occur, leading to toxicity.

Pharmacokinetics in Children

Biological maturity and growth gradually enable the drug response of children to approximate that of adults. Physiological changes that influence these responses: increase in body mass, fat content increases, percentage of body water volume decreased, number of plasma-proteins for drug binding increases, and the blood-brain barrier and skin become more effective drug barriers. Growth spurts during childhood and adolescence also effect drug response.

Absorption:

- Gastric pH in children does not approximate adult values until 2nd or 3rd year of age. Until then, this relative lack of acidity results in increased absorption of medications that are normally inactivated by gastric acid.
- Gastric emptying rates are faster than in infants, enabling drugs to move more rapidly to the small intestine where absorption is enhanced.
- The skin and blood-brain barrier becomes more effective, making the child less vulnerable to drug toxicities.

Distribution:

- The concentration of plasma proteins reaches adult levels by approximately age 1. This means that more of the drug can bind to the increased number of protein-binding sites in 1-year-olds as compared to infants, resulting in a decreased distribution of active drug
- Children up to age 2 continue to have a higher relative body water content compared to older children, and therefore may require higher doses of water-soluble drugs than those over age 2.

Metabolism:

- As children mature, liver enzymes are able to effectively metabolize most drugs, because the BMR in children is higher than in adults, drugs are metabolized more quickly. thus drug dosages relative to body weight may need to be higher for children than adults.
- Drug dosages for drugs that metabolized very quickly in some children, (e.g., Theophylline) should be tailored to the individual based on drug levels and clinical response.

Excretion:

- Children over 12 months of age are able to excrete drugs effectively from their more mature kidneys, preventing drug effects from lasting too long.